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# Refractory Sideroblastic and Nonsideroblastic Anemia

## A REVIEW OF 27 CASES

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*A study was done with 27 patients who met the following criteria: (1) anemia, (2) cellular bone marrow not diagnostic of leukemia, (3) absence of underlying disease that could account for the hematologic abnormalities at time of initial study and (4) absence of iron, $B_{12}$ or folate deficiency.*

*Of the 27 patients, 13 had ringed sideroblasts and 14 did not. Eleven patients received corticosteroids, 18 received folate, 23 pyridoxine and 12 androgens. Two partial responses occurred in the sideroblastic group and were attributed to androgen therapy in one patient and pyridoxine therapy in the other. In the nonsideroblastic group, two partial responses occurred which were attributed to prednisone therapy. Transfusions were required in 23 patients. Leukemia developed in six patients.*

*It is concluded that currently used treatments have little effect on refractory anemia and that in most patients continuing transfusions are required. In a small percentage of patients, there is transformation to leukemia.*

REFRACTORY ANEMIA with normoplastic or hyperplastic marrow is a primary bone marrow disorder of unknown cause. It is generally unresponsive to specific forms of therapy such as administration of folic acid, vitamin $B_{12}$ or iron, and at best is only partially responsive to treatment with androgens, pyridoxine and corticosteroids. It is often associated with leukopenia or thrombocytopenia, or both. This type of anemia has been variously referred to by designations such as primary refractory anemia, refractory normoblastic anemia,[1] refractory sideroblastic anemia,[2] pancytopenia with cellular marrow, chronic bone marrow failure,[3] refractory anemia with hyperplastic bone marrow and aregenerative anemia.[4] It should be distinguished from true aplastic anemia, in which the early stage may be associated with islands of active hematopoiesis, and from the congenital dyserythropoietic anemias which are characterized by erythroid multinuclearity and which may have associated cytopenias.[5]

Refractory anemia may be subdivided into two general categories: nonsideroblastic and sideroblastic. The purpose of this paper is to review the natural history of 27 cases of refractory sideroblastic and nonsideroblastic anemia.

### Patients and Methods

All patients with anemia of at least a year's duration who were seen at the City of Hope Medical Center between 1958 and 1975 were

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considered for inclusion in this study. Those patients in whom there were bone marrow findings diagnostic of leukemia or bone marrow aplasia when first seen, in whom systemic disease was found which might account for the anemia or in whom a deficiency was present in iron, vitamin $B_{12}$ or folic acid were excluded.

First, histories were taken and physical examinations carried out in all patients who met the criteria enumerated above. With few exceptions the following studies also were done in all cases: x-ray studies of the chest, renal function studies, electrocardiograms and determinations of serum iron and iron binding capacity, blood glucose and uric acid. Hematologic studies included hemoglobin, red cell count, hematocrit, leukocyte count and differential, and platelet and reticulocyte counts. A minimum of two bone marrow examinations were done in all cases. Bone marrow specimens were obtained by aspiration from the sternum or iliac crest. Films were stained with Wright-Giemsa stain. To evaluate iron stores the Prussian blue reaction was used on both smears and sectioned aspirates. Sections were also stained with hematoxylin and eosin. Chromosome analysis of marrow cells or peripheral blood, or both, was done in nine patients.

## Results

A total of 27 patients fulfilled the criteria for inclusion in the study. Each patient was classified as either sideroblastic or nonsideroblastic; 13 of the 27 patients had ringed sideroblasts and 14 did not. In the sideroblastic group there were 8 white males, 1 black male and 4 white females. At time of diagnosis the age range was from 6 to 79 years, with a median age of 62 years and a mean age of 60 years. In the nonsideroblastic group there were 9 white females and 5 white males. At time of diagnosis the age range was from 29 to 84 years, the median age 52 years and the mean age 54 years. The results of some of the physical findings and laboratory results are summarized in Table 1.

### *Physical Findings*

Patients in both groups presented with the usual signs and symptoms of anemia. In the group of 13 patients with sideroblastic anemia, the liver was palpable in eight, extending from 1 to 6 cm below the right costal margin, and in two of the 13 patients splenomegaly was present, with the spleen palpable 3 to 7 cm below the left costal margin. In the group of 14 patients with nonsideroblastic anemia, the liver was palpable in eight, extending from 1 to 11 cm below the right costal margin and in five of the 13 patients splenomegaly was present, with the spleen palpable 2 to 5 cm below the left costal margin.

### *Blood Counts and Laboratory Findings*

When the 13 patients with sideroblastic anemia were first seen at the City of Hope Medical Center, hemoglobin levels ranged from 7.1 to 12.5 grams per 100 ml (after transfusion), leukocyte counts from 2,500 to 10,450 per cu mm and platelets from 162,000 to 900,000 per cu mm. The reticulocyte counts in 11 of the 13 patients were low or normal, and increased in two cases. Serum iron levels were measured in ten of the 13 patients and all were in the upper range of normal or elevated. Uric acid levels were elevated in four of the 12 for whom determinations were carried out.

When the 14 patients with nonsideroblastic anemia were first seen at the City of Hope Medical Center, hemoglobin levels ranged from 4.4 to 11.4 grams per 100 ml, leukocyte counts from 1,600 to 6,900 per cu mm and platelets from 9,500 to 500,000 per cu mm. Reticulocyte counts

TABLE 1.—*Comparison of Features of Sideroblastic and Nonsideroblastic Anemia**

| | | *Sideroblastic* | *Nonsideroblastic* |
|---|---|---|---|
| Spleen (palpable) | | 2/13 patients | 5/14 patients |
| Liver (palpable) | | 8/13 patients | 8/14 patients |
| Hemoglobin level | mean | 8.9 grams per 100 ml | 7.8 grams per 100 ml |
| | median | 9.1 grams per 100 ml | 7.5 grams per 100 ml |
| Reticulocyte count | mean values | 1.13 percent | 1.24 percent |
| Leukocyte count | | 5,281 per cu mm | 4,510 per cu mm |
| Platelets | | 318,000 per cu mm | 222,000 per cu mm |
| Serum iron | | 207 mg per 100 ml | 168 mg per 100 ml |
| Serum iron-binding capacity | | 317 mg per 100 ml | 336 mg per 100 ml |
| Uric Acid | | 6.6 mg per 100 ml | 6.4 mg per 100 ml |

*All measurements represent initial values when patients were first seen at City of Hope.

in 11 of the 14 patients were normal or low, and increased in three cases. Serum iron levels were measured in seven of the 14 patients, and all were in the middle to high normal range or elevated. Uric acid levels were elevated in three of the 12 patients for whom determinations were done.

*Bone Marrow Findings*

In the sideroblastic group, increased erythropoiesis was present in the marrow of 12 of the 13 patients. In 12 of the 13 patients increased iron stores were noted. Megakaryocytes were normal or increased in number and myelopoiesis was decreased, normal or increased.

On bone marrow examination in the nonsideroblastic group of 14 patients, varied erythroid, myeloid and megakaryocytic activity was found. Iron stores were increased in most of the cases but were normal or initially decreased in several patients.

*Karyotypes*

Bone marrow karotypes were done in four of the sideroblastic cases, with three yielding normal results. In the fourth patient (patient 6) there was an initially normal karyotype in 1965 but a later karyotype in 1966 had pseudodiploidy and evidence of chromatid breaks, monosomy for chromosome #20 and an abnormal metacentric chromosome.

In five patients in the nonsideroblastic group, bone marrow karyotypes were done. The result was normal in one case, but in the remaining four the following separately encountered abnormalities were present: pseudodiploidy, chromosome breaks, long-arm deletion and aneuploidy.

*Treatment and Course*

In the sideroblastic group, 3 patients were treated with corticosteroids, 9 with folate, 13 with pyridoxine and 5 with androgens. Four of the 13 patients treated with pyridoxine received it before coming to City of Hope. The remaining nine patients treated with pyridoxine received it in a range of 50 to 400 mg per day from 1.5 months to ten years, with the exception of 1 patient who received 200 mg per day for three weeks. Two patients received experimental treatment, one with cytosine arabinoside given intravenously (6 five-day courses of 1 to 2 mg per kg of body weight per day), and one with pyridoxal phosphate given intramuscularly (250 mg per day for ten days). Eleven of the 13 patients did not respond to treatment. In one patient (patient 11) there was a transient, modest rise in the hemoglobin level following androgen therapy, but this partial response was terminated by the development of Coombs positive hemolysis necessitating treatment with prednisone. Thereafter, infrequent transfusions have been required. In another patient (patient 3) there was a mild rise in the hemoglobin value following pyridoxine therapy. In patient 4 there was a brief reticulocytosis while pyridoxine was being given but no rise in the hemoglobin value. Twelve of 13 patients received multiagent therapy. Transfusions were required in nine patients.

Patients in the nonsideroblastic group were treated as follows: 8 received corticosteroids, 9 folate, 10 pyridoxine, 2 vitamin $B_{12}$, 2 cobaltous chloride, 7 androgens and 1 received only transfusion therapy. Four of the ten patients treated with pyridoxine received it before coming to City of Hope. The remaining six patients received pyridoxine in a range of 150 to 600 mg per day for from three months to two years. Two patients received cytoxan (range of 50 to 150 mg per day given by mouth for about 1 to 2 months), four patients received cytosine arabinoside intravenously (1 to 4 five-day courses of 1 to 2 mg per kg of body weight per day), one patient received thioguanine (100 mg by mouth every day for five days) and one patient received 6-mercaptopurine (25 mg by mouth every day for five days) as experimental therapy. In 12 of 14 patients no significant response to treatment was seen, although in 2 patients (patients 19 and 25) there was a brief reticulocytosis without a rise in hemoglobin values during pyridoxine therapy. Two patients entered partial remission. Prednisone was considered a possible cause of one partial remission (patient 14). Before prednisone was used, the patient was treated with androgens, vitamin $B_{12}$, folate, iron, pyridoxine, cobaltous chloride, Valentine's liver extract, adenine, cytosine and cytodylic acid without benefit.

The other patient (patient 21) entered partial remission while receiving long-term prednisone therapy two years after receiving cytosine arabinoside. Twelve of 14 patients received multiagent therapy. Transfusions were required in all patients in the nonsideroblastic group. Fewer than half the patients in the two combined groups were treated with iron or vitamin $B_{12}$ (or both) before evaluation at the City of Hope Medical Center.

TABLE 2.—*Patients with Sideroblastic Anemia*

| *Patient, Race and Sex* | *Year Anemia Dx* | *Age at Dx* | *Hb gms per 100 ml Retic. Count Percent* | *Leukocytes/ cu mm* | *Platelets ×1,000/ cu mm* | *Outcome* | *Serum (μg per 100 ml) Fe* | *Serum (μg per 100 ml) IBC* | *Initial Marrow (Sideroblastic)* | *Uric Acid* | *Transfusions* | *Karyotype* | *Liver Cm* | *Spleen Cm* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1W♂ | ... 1957 | 43 | 9.8<br>1.0 | 3,500 | 179 | Stable without treatment | 287 | 315 | E↑MK→MY↓I↑ | 6.5 | 0 | ..... | 0 | 0 |
| 2W♀ | ... 1959 | 62 | 9.6<br>1.1 | 4,500 | 360 | Stable without treatment | 194 | 332 | E↑MK→MY↓I↑ | 3.0 | 3 | ..... | 1 | 0 |
| 3W♂ | ... 1959 | 6 | 7.6<br>0.4 | 10,450 | 900 | Stable without treatment | 246 | 520 | E↑MK↑MY→I→ | 3.8 | 5 | Normal male 46 XY | 3 | Abst. |
| 4W♂ | ... 1963 | 58 | 9.3<br>5.4 | 4,000 | 205 | No response to treatment | 275 | 280 | E↑MK→MY→I↑ | 7.2 | 0 | Normal male 46 XY | 2 | 3 |
| 5W♀ | ... 1964 | 58 | 7.3<br>2.3 | 4,300 | 196 | Stable without treatment | 159 | 202 | E↑MK↑MY→I↑ | 6.0 | 0 | ..... | 2 | 0 |
| 6W♀ | ... 1965 | 76 | 7.4<br>.. | 4,400 | 217 | No response to treatment | 160 | 165 | E↑MK→MY↑I↑ | 13.8 | 29 | Normal female 1965<br>Abnormal 1966<br>(see text) | 0<br>↓<br>6 | 0<br>↓<br>7 |
| 7W♂ | ... 1966 | 54 | 7.4<br>0.1 | 6,800 | 510 | Died 1970, acute leukemia | 242 | 500 | E↑MK↑MY→I↑ | .. | 57 | ..... | 6 | 0 |
| 8W♂ | ... 1968 | 68 | 10.7<br>1.0 | 7,300 | 230 | Died 1971, myocardial infarction | 190 | 300 | E↑MK→MY→I↑ | 9.7 | 44 | ..... | 6 | 0 |
| 9W♀ | ... 1969 | 78 | 12.5*<br>0* | 4,900 | 225 | Died 1971, myocardial infarction | .. | .. | E→MK↑MY↑I↑ | 3.9 | ? | ..... | 0 | 0 |
| 10W♂ | ... 1970 | 79 | 10.9<br>0.3 | 6,300 | 322 | Died 1974, congestive heart failure, arterio-sclerotic heart disease | .. | .. | E↑MK↑MY→I↑ | 4.2 | 52 | ..... | 2<br>↓<br>6 | 0 |
| 11W♂ | ... 1972 | 69 | 9.1<br>1.1 | 4,500 | 246 | Continuing transfusion requirement | .. | .. | E↑MK↑MY→I↑ | 4.2 | ? | Normal male 46 XY | 0 | 0 |
| 12B♂ | .... 1973 | 61 | 7.1<br>0.2 | 2,500 | 162 | Continuing transfusion requirement | 188 | 262 | E↑MK↑MY→I↑ | 7.7<br>↓<br>8.6 | 27 | ..... | 0 | 0 |
| 13W♂ | ... 1974 | 68 | 7.9<br>0.6 | 5,200 | 380 | No response to treatment | 133 | 294 | E↑MK→MY→I↑ | 8.4 | 0 | ..... | 0 | 0 |

*Immediately after transfusion.

E = Erythropoiesis
Hb = Hemoglobin
MK = Megakarocytes
MY = Myelopoiesis
I = Iron
IBC = Iron-binding capacity
↑ = Increase
→ = Normal
↓ = Decrease
W = White
B = Black

TABLE 3.—*Patients with Nonsideroblastic Anemia*

| *Patient, Race and Sex* | *Year Anemia Dx* | *Age at Dx* | *Hb gms per 100 ml Retic. Count Percent* | *Leukocytes/ cu mm* | *Platelets ×1,000/ cu mm* | *Outcome* | *Serum (μg per 100 ml) Fe* | *Serum (μg per 100 ml) IBC* | *Initial Marrow (Nonsideroblastic)* | *Uric Acid* | *Transfusions* | *Karyotype* | *Liver Cm* | *Spleen Cm* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 14W♀ | ... 1956 | 29 | 5.8<br>1.4 | 4,550 | 86 | Entered partial remission 1968 | 153 | 290 | E↑MK↓MY→I→ | 3.9 | 26 | ..... | 0 | 0 |
| 15W♀ | ... 1957 | 51 | 4.4<br>0.4 | 3,850 | 500 | Died 1975, congestive heart failure (hemochromatosis) | 153 | 358 | E↓MK↑MY→I↑ | 6.1 | 229 | ..... | 2<br>↓<br>8 | 0<br>↓<br>5 |
| 16W♀ | ... 1964 | 29 | 8.8<br>0.2 | 4,950 | 165 | Died 1971, unrelated cause | .. | .. | E↓MK→MY↑I↑ | .. | 7 | ..... | 1 | 0 |
| 17W♀ | ... 1965 | 41 | 11.4<br>0.6 | 6,900 | 176 | Died 1975, acute leukemia | 140 | 318 | E→MK↑MY→I→ | 3.9 | ? | Deleted long arm of chromosome #5 | 8 | 3 |
| 18W♀ | ... 1970 | 84 | 11.3<br>0.5 | 4,100 | 70 | Died 1972, acute leukemia | .. | .. | E↑MK↑MY→I→ | .. | 71 | ..... | 6 | 0 |
| 19W♂ | ... 1970 | 48 | 9.2<br>0.6 | 4,100 | 340 | Died 1975, acute leukemia | 106 | 235 | E↑MK↑MY↑I↓↑ | 5.3 | 50 | 46 XY Pseudodiploidy | 2<br>↓<br>5 | 2<br>↓<br>4 |
| 20W♀ | ... 1970 | 65 | 8.6<br>4.2 | 6,400 | 380 | Died 1975, ? cause | 6 | 0 | E→MK↑MY↑I↑ | 9.6 | ? | ..... | 0 | 0 |
| 21W♂ | ... 1971 | 34 | 6.9<br>0.4 | 1,600 | 9.5 | Entered partial remission 1975 | 255 | 678 | E↑MK↓MY↓I↓↑ | 4.5 | 115 | ..... | 0 | 0 |
| 22W♂ | ... 1971 | 62 | 6.8<br>0.5 | 6,100 | 275 | Transformation to chronic myelomonocytic leukemia, died 1976 | .. | .. | E↓MK→MY↑I? | 4.6 | 135 | ..... | 11 | 5 |
| 23W♀ | ... 1971 | 58 | 7.1<br>0.2 | 3,400 | 120 | Died 1974, unrelated cause | .. | .. | E↓MK↓MY→I↑ | 4.4 | 96 | ..... | 0<br>↓<br>5 | 2 |
| 24W♀ | ... 1973 | 70 | 7.8<br>0.2 | 4,100 | 300 | Died 1975, unrelated cause | 177 | 228 | E↑MK→MY↓I↑ | 10.0 | 59 | No specific chromosome abnormalities | 3 | 0 |
| 25W♂ | ... 1973 | 51 | 5.4<br>3.5 | 5,200 | 415 | Transfusion requirements continue | 191 | 244 | E↑MK→MY→I↑ | 14.2 | 45 | 2 out of 22 cells had breaks in one of the chroms (9%) | 0 | 0 |
| 26W♀ | ... 1974 | 54 | 7.2<br>4.4 | 5,500 | 124 | Transfusion requirements continue | .. | .. | E↑MK→MY↑I↑ | 4.8 | 6 | 14% aneuploidy | 0 | 0 |
| 27W♂ | ... 1974 | 79 | 7.8<br>0.3 | 2,400 | 152 | Died acute leukemia 1975 | .. | .. | E↓MK↓MY↑I↑ | 5.8 | 8 | ..... | 0 | 0 |

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↓ = Decrease
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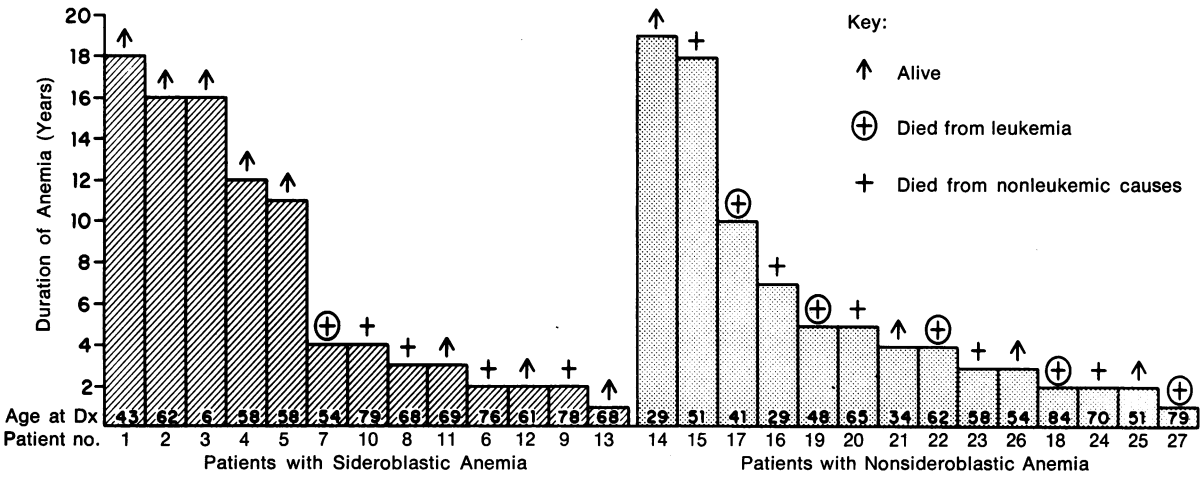


**Figure 1.**—Duration of anemia and outcome of 27 cases of refractory anemia.

The clinical course of each patient is summarized in Tables 2 and 3. Figure 1 shows a comparison of the duration of anemia in the 27 patients. In the nonsideroblastic group acute leukemia developed in four patients, in one of whom (patient 17) anemia had been present for ten years. In one patient (patient 22) in the nonsideroblastic group chronic myelomonocytic leukemia developed. In only one patient in the sideroblastic group did acute leukemia develop. However, two patients with sideroblastic refractory anemia were not entered into the study because acute leukemia had developed in each within less than a year after anemia developed; therefore they did not fulfill the criteria used in selecting patients for this survey.

## Discussion

The major feature that distinguishes primary acquired refractory anemia from aplastic anemia is the degree of bone marrow cellularity; in the former the marrow ranges from normocellular to intensely hypercellular, whereas in the latter the marrow is almost devoid of hematopoietic tissue. Patients with primary acquired refractory anemia may be classified as having either refractory sideroblastic anemia or refractory nonsideroblastic anemia. Studies of the bone marrows of patients with sideroblastic anemia show the presence of numerous normoblasts containing large amounts of stainable iron arranged in a ring surrounding the nucleus. These cells, the so-called "ringed sideroblasts," contain mitochondria which are distended with nonferritin iron; in contrast, normoblasts from normal subjects contain iron primarily in the form of cytoplasmic ferritin aggregates.[9]

An important feature common to both sideroblastic and nonsideroblastic anemia is ineffective erythropoiesis. Dacie and co-workers studied seven cases of sideroblastic anemia and showed there to be poor utilization of intravenously administered radioactive iron ($^{59}Fe$): there was subnormal delivery of tagged red cells into the peripheral blood in conjunction with a rapid turnover of iron in the plasma.[1] Sultan reported that the bone marrows of six patients with refractory anemia were incapable of forming colonies *in vitro* on agar gel medium and in that respect acted as do bone marrows from patients with acute myelogenous leukemia in relapse.[6]

Leukopenia or thrombocytopenia (or both) may coexist with the anemia. White cell abnormalities that have been reported include: Pelger-Huêt granulocytes, granulation defects in polymorphonuclear leukocytes, occasional immature granulocytes, monocytosis, atypical monocytes and bizarre platelets.[7] Platelet adhesiveness and aggregation abnormalities have been reported in cases of sideroblastic anemia.[8]

Observations on 35 patients with primary sideroblastic anemia were published by MacGibbon and Mollin.[10] Three of the patients were boys with hereditary sex-linked anemia. However, most of the patients were elderly, with an average age of 70 years; 60 percent were female. Characteristic hematological features included low reticulocyte percentage, pronounced erythroid hyperplasia, often megaloblastic, serum iron and percentage saturation of total iron-binding capacity frequently raised, and an insignificant decrease or no decrease in mean red cell lifespan. Pyri-

doxine therapy (1 to 100 mg per day) was used in 27 patients. In 37 percent there was hematologic response, frequently only partial but occasionally almost complete (a hemoglobin level at least 14 grams per 100 ml, but with hypochromic red blood cells and persistence of ring sideroblasts).

Our observations are similar with regard to reticulocyte percentage, degree of erythroid hyperplasia of the marrow and serum iron studies. The response to therapy of our patients was strikingly different from that reported by MacGibbon and Mollin, however. In our group only two of 13 sideroblastic patients responded and only partially, one to androgens and the other to pyridoxine therapy.

A study of ten cases of refractory sideroblastic anemia was reported by Barry and Day.[11] Two patients had splenomegaly and 3 had hepatomegaly. The hemoglobin levels ranged from 5 to 10 grams per 100 ml. The initial leukocyte counts were low in five patients, the lowest level being 2,700 per cu mm. Platelet levels were low, normal or elevated. Folate treatment did not significantly change the basic features. Six patients received transfusion therapy. One patient with a history of exposure to benzol died of acute monoblastic leukemia 13 years after anemia was first discovered. In our group of 13 sideroblastic patients we found that a smaller percentage had splenomegaly and a larger percentage hepatomegaly. Hemoglobin values, white cell counts and platelet levels were similar in the two groups. Folate therapy was of no significant benefit in either group. In both series of sideroblastic patients there was one who died from acute leukemia. In most of the patients in both groups transfusion therapy was required.

Kushner and associates reported the results of clinical and laboratory investigations of 17 patients with idiopathic refractory sideroblastic anemia.[12] The age range was from 54 to 88 years. At the time of initial physical examination the liver was palpable in seven patients and the spleen was palpable in five patients. In the 17 patients the hematocrit reading ranged from 22 to 38 percent. Erythroid hyperplasia of the marrow and increased marrow iron were characteristic. Hyperferremia was present in 12 of the 17 patients at the time of initial study. In seven patients periodic transfusions were required. Nine patients received androgens alone or in combination with prednisone for a minimum of three months. In three of the nine patients there was significant improvement. Ten patients received pyridoxine (50 to 200 mg per day) and none responded. One patient died with acute myeloblastic leukemia seven years after the onset of sideroblastic anemia.

The age range of our patients was somewhat younger. Similarities include bone marrow patterns and serum iron levels. A higher percentage of patients in our group required periodic transfusions. Fewer of our patients responded to drug therapy but the infrequent response to pyridoxine in the series of Kushner and co-workers parallels our experience and stands in contrast to the high frequency of response reported by MacGibbon and Mollin.[10]

The heterogeneity of refractory anemia with hyperplastic bone marrow was emphasized by Vilter and associates, who separated patients into five types.[13]

It has been considered that the first stage of Di Guglielmo syndrome (erythremic myelosis) is frequently identical to sideroblastic anemia.[14] Di Guglielmo syndrome may exist in a chronic form beginning as a refractory anemia (preleukemia) and terminates years later as leukemia.[15] Block and associates listed primary refractory anemia with hyperplastic marrow among the differential diagnoses which may be considered in the preleukemic phase of acute leukemia.[16] Bauters and co-workers reported that out of a series of 15 cases of refractory anemia, the condition transformed to acute myeloblastic leukemia in five patients. Two of the 15 patients had sideroblastic anemia and were not among those in whom acute leukemia developed.[17]

In our series of 13 sideroblastic patients, acute leukemia developed in one, whereas in the 14 nonsideroblastic patients acute leukemia developed in four and chronic myelomonocytic leukemia in one (patient 22).

Chromosome abnormalities are known to occur in refractory anemia. In a series of six cases of acquired sideroblastic anemia, five patients were found to have abnormalities. In two cases a partial deletion of an arm of a chromosome 19-20 occurred and in three cases a rearrangement of a chromosome 19-20, which probably represented pericentric inversion was shown to have occurred.[18]

In our series of 27 cases of refractory anemia, chromosome analysis was done in nine patients.

In five the karyotype was normal; however, a later change to abnormal occurred in one patient (patient 6, sideroblastic).

We conclude that patients with refractory sideroblastic and nonsideroblastic anemia have a highly variable course with regard to duration of anemia (Table 3). In most cases transfusion requirements develop. Responses to forms of therapy such as androgens, pyridoxine, folate and corticosteroids occur infrequently and are partial, at best. In a small percentage of patients, transformation to acute leukemia occurs and this may happen even after many years.

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## The Relationship Between Colorectal Polyps and Carcinoma

DR. TROLLOPE: "Yes, indeed, there is a relationship between polyps and carcinoma, and this seems true not only for the villous adenomas that we have agreed upon in the past, but also for even small adenomatous polyps. . . . Second, any patient with any size polyp shown on barium enema should be considered for colonoscopic polypectomy. Third, colon resection for polyps with carcinoma is indicated only in certain circumstances (when it is down in the base, when it is in the lymphatics, and so on). Finally, in every patient after polypectomy has been done a barium enema study and sigmoidoscopy should be carried out yearly until five consecutive examinations have given normal findings."

—MICHAEL L. TROLLOPE, MD, *Palo Alto, CA*

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